

CLAIMS

1. A method for preparing a peptide antigen with modulated immunogenicity comprising substituting at least a first amino acid located in a CTL epitope with a first substitute amino acid having an extended or shortened side chain as compared to the first amino acid.
2. The method of claim 1, wherein the first substitute amino acid has the same base residue as the first amino acid.
3. The method of claim 1, wherein the first substitute amino acid is a non-natural amino acid.
4. The method of claim 1, wherein the side chain is an aliphatic side chain.
5. The method of claim 1, wherein the first substitute amino acid extends the side chain.
6. The method of claim 5, wherein the first substitute amino acid adds a —CH₂/CH₃ group to the side chain.
7. The method of claim 5, wherein the first substitute amino acid adds two —CH₂/CH₃ groups to the side chain.
8. The method of claim 1, wherein the first substitute amino acid shortens the side chain.
9. The method of claim 8, wherein the first substitute amino acid reduces one —CH₂/CH₃ group on the side chain.
10. The method of claim 8, wherein the first substitute amino acid reduces two —CH₂/CH₃ groups on the side chain.
11. The method of claim 4, wherein the first substitute amino acid eliminates an —OH group from the side chain.
12. The method of claim 4, wherein the first substitute amino acid eliminates an —NH₂ group from the side chain.

13. The method of claim 4, wherein the first substitute amino acid adds an $-NH_2$ group to the side chain.
14. The method of claim 1, further comprising determining the CTL epitope of the antigen.
- 5 15. The method of claim 1, further comprising modeling the CTL epitope while bound in the MHC-1 groove.
16. The method of claim 1, further comprising modeling the CTL epitope while bound in the MHC-II groove.
- 10 17. The method of claim 1, further comprising substituting a second amino acid located in the CTL epitope with a second substitute amino acid having an extended or shortened side chain as compared to the second amino acid.
18. The method of claim 17, further comprising substituting a third amino acid located in the CTL epitope with a third substitute amino acid having an extended or shortened side chain as compared to the third amino acid.
- 15 19. The method of claim 18, further comprising substituting a fourth amino acid located in the CTL epitope with a fourth substitute amino acid having an extended or shortened side chain as compared to the fourth amino acid.
- 20 20. The method of claim 1, wherein the antigen is a tumor antigen.
21. The method of claim 20, wherein the tumor antigen is derived from breast cancer, ovarian cancer, prostate cancer, blood cancer, skin cancer, uterine cancer, cervical cancer, liver cancer, colon cancer, lung cancer brain cancer, head & neck cancer, stomach cancer, esophageal cancer, pancreatic cancer, or testicular cancer.
22. The method of claim 21, wherein the tumor antigen is HER-2.
- 25 23. The method of claim 1, wherein the antigen is a viral antigen.
24. The method of claim 1, wherein the antigen is a bacterial antigen.
25. The method of claim 1, wherein the antigen is a parasitic antigen.

26. The method of claim 1, wherein modulation of immunogenicity comprises an increase in the antigen's ability to selectively activate high-avidity CTL precursors.
- 5 27. The method of claim 1, wherein modulation of immunogenicity comprises an increase in the antigen's ability to activate low-avidity CTLs.
28. The method of claim 1, wherein modulation of immunogenicity comprises an increase in the antigen's ability to protect CTLs from activation induced cell death.
- 10 29. The method of claim 1, wherein modulation of immunogenicity comprises an increase in the antigen's ability to selectively activate cytokine production.
30. The method of claim 1, wherein modulation of immunogenicity comprises an increase in the antigen's ability to induce CTL proliferation.
31. The method of claim 1, wherein the substitution increases the affinity of the antigen for a T cell receptor.
- 15 32. The method of claim 1, wherein the substitution reduces interactions that interference with T cell receptor binding.
33. A method of inducing immunity in a subject comprising administering to said subject a modified peptide antigen comprising a CTL epitope, wherein said antigen has at least one amino acid with a length-modified side chain, as compared to the same position in the natural molecule, within the CTL epitope.
- 20 34. The method of claim 33, wherein the subject is a human.
35. The method of claim 33, wherein said modified peptide antigen is a modified tumor peptide antigen.
- 25 36. The method of claim 33, wherein the length-modified side chain is extended as compared to the same position in the natural molecule.

37. The method of claim 33, wherein the length-modified side chain is shortened as compared to the same position in the natural molecule.
38. The method of claim 33, wherein the modified peptide comprises a second amino acid with a length-modified side chain.
- 5 39. The method of claim 33, wherein the modified peptide comprises a third amino acid with a length-modified side chain.
40. The method of claim 33, wherein the modified peptide comprises a fourth amino acid with a length-modified side chain.
- 10 41. A method of treating a HER-2 related cancer comprising administering to said subject a modified E75 peptide, wherein said peptide has at least one amino acid with a length-modified side chain, as compared to the same position in the natural molecule.
42. The method of claim 41, wherein the HER-2 related cancer is breast or ovarian cancer.
- 15 43. A peptide antigen with modulated immunogenicity prepared according to the method of claim 1.